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OXIDATION OF 3,4-DIHYDROISOQUINOLINIUM SALTS WITH DMSO/conc HCl

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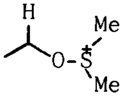
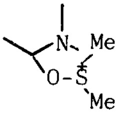
Abstracts: 3,4-Dihydroisoquinolinium salts can be oxidized to the corresponding isoquinolones by DMSO in conc HCl.

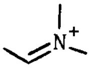
Apart from its special solvent power, DMSO has been used extensively for the oxidation of various organic compounds. One reaction utilizing DMSO in the oxidation of alkyl halide or tosylate is an oxidative process known as the Kornblum oxidation. The oxidation proceeds through the intermediacy of the oxysulfonium salt (I) which fragments to give the carbonyl compound and dimethyl sulfide as by product. The oxysulfonium derivative can also be generated by other pathways[1]. It occurred to us that the oxysulfonium intermediate (II) might also be formed by the reaction of DMSO with iminium salt (III) because of the electrophilic property of the iminium group.



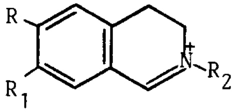
I



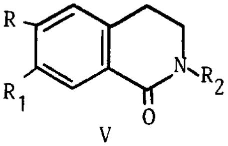
II



III



IV

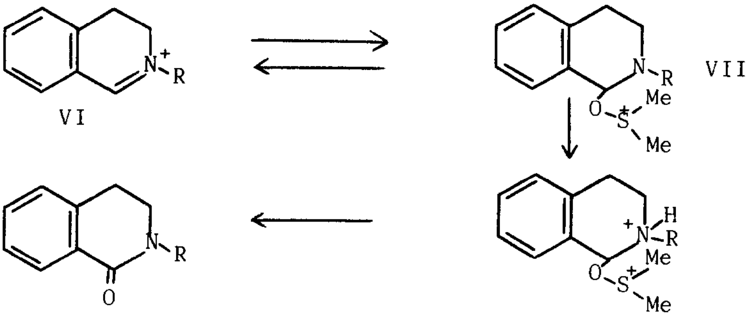


V

		% yield	NMR ($CDCl_3$) C-8 ArH
a)	R = R_1 = OMe R_2 = Me	86	7.65(s)
b)	R = R_1 = OMe R_2 = Bz	45	7.70(s)
c)	R = R_1 = OMe R_2 = 2-(3,4-dimethoxyphenylethyl)	75	7.76(s)
d)	R + R_1 = O-CH_2O R_2 = Me	85	7.53(s)
e)	R = R_1 = H R_2 = Me	82	8.10(m)

We found that DMSO in conc.HCl[2] could be effectively used for the oxidation of various 3,4-dihydroisoquinolinium salts to the corresponding isoquinolones. The reaction can be carried out simply by dissolving 3,4-dihydroisoquinolinium salts in DMSO followed by addition of conc.HCl. For example, N-methyl 3,4-dihydro-6,7-dimethoxyisoquinolinium iodide (IVa) was dissolved in DMSO and conc HCl was added (ratio of DMSO/conc.HCl = 7). After the solution was stirred at room temperature for 1 h., N-methyl-3,4-dihydro-6,7-dimethoxy-1-isoquinolone (Va) was isolated in 86 % yield by preparative layer chromatography. Other compounds (IVb-IVe) could be smoothly oxidized to the corresponding isoquinolones[3] (Vb-Ve) by the same procedure. In absence of acid, no oxidation took place. When 2N HCl was used a lower yield was obtained, for example, oxidation of compound IVa with DMSO and 2N HCl for 1 h. gave isoquinolone Va in 45 % yield and longer period (overnight) oxidation gave a better yield (66 % yield).

The oxidation was also performed in the presence of bases (Na$_2$CO$_3$ and NaHCO$_3$), however the yield of the isoquinolone was much lower. It was most likely that DMSO was not involved in the oxidation, and the reaction occurred by a different pathway[4]. The requirement of HCl led us to propose the following mechanism.



Nucleophilic addition of DMSO to the iminium salt (VI) leads to the oxysulfonium intermediate (VII). This reaction is reversible and the main product is the iminium salt in DMSO alone. However, upon adding HCl to the solution, the lone pair electrons on nitrogen wiil be protonated rendering the reaction irreversible. Loss of a proton followed by cleavage of oxygen-sulfur bond (or the reversed process) can then lead to the product. Analagous oxidation of iminium salts with peracid[5] or pyridine N-oxide[6] is known.

References and Notes

1) For a review see: A.H. Haines, Chem. & Ind., 883 (1976) and references cited therein.

2) DMSO in conc.HCl has previously been used for the oxidation of indole derivatives, W.E. Savige and A. Fontana, J. C. S. Chem. Comm., 599 (1976), K. Szabo-Pusztay and L. Szabo, Synthesis 276 (1979)

3) All products were isolated by preparative layer chromatography and fully characterized.

4) S. Ruchirawat, S. Sunkul, Y. Thebtaranonth, and N. Therasasna, Tetrahedron Lett., 2335 (1977)

5) H.H. Wasserman and A.W. Tremper, Tetrahedron Lett., 1449 (1977)

6) R. Da Costa, M. Gillard, J.B. Falmagne, and L. Ghosez, J. Amer. Chem. Soc. 101, 4381 (1979)

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